

polynucleotide that encodes a cell-specific ligand that specifically binds to a protein on the surface of a cell of interest, wherein the first and second forms of each nucleic acid differ from each other in two or more nucleotides, to produce a library of recombinant binding moiety-encoding nucleic acids;

(2) producing a library of vectors from the library of recombinant binding moiety-encoding nucleic acids, wherein each vector comprises: a) a binding site specific for the nucleic acid binding domain and b) a member of the library of recombinant binding moiety-encoding nucleic acids;

(3) introducing one or more members of the library of vectors into one or more host cells, wherein the encoded recombinant binding moiety is expressed and recovering the expressed recombinant binding moiety;

(4) binding the expressed recombinant binding moiety to a vector comprising the binding site to form a vector-binding moiety complex;

(5) contacting the vector-binding moiety complex with a target cell of interest; and

(6) determining if one or more target cells contain a vector from the vector-binding moiety complex, and recovering the recombinant cell-specific binding moiety nucleic acid from any such target cells.

3. (Twice Amended) The method of claim 2, wherein the method further comprises:

(7) recombining at least one recombinant binding moiety-encoding nucleic acid of (6) with a further form of the polynucleotide that encodes a nucleic acid binding domain and/or a further form of the polynucleotide that encodes a cell-specific ligand, which are the same or different from the first and second forms, to produce a further library of recombinant binding moiety-encoding nucleic acids;

(8) producing a further library of vectors from the further library of recombinant binding moiety-encoding nucleic acids, wherein each vector in the further library of vectors comprises: a) a binding site specific for the nucleic acid binding domain and b) a member of the further library of recombinant binding moiety-encoding nucleic acids;

(9) introducing one or more members of the further library of vectors into one or more host cells, wherein the encoded recombinant binding moiety is expressed and recovering the expressed recombinant binding moiety;

(10) binding the expressed recombinant binding moiety of (9) to a vector comprising the binding site to form a vector-binding moiety complex;

(11) contacting the vector-binding moiety complex of (10) with a target cell of interest and determining if one or more target cells contain a vector from the vector-binding moiety complex of (10);

(12) recovering the recombinant binding moiety-encoding nucleic acid from any such target cells of (11); and

(13) repeating (7) through (12) to screen for a cell-specific binding moiety useful for increasing uptake or specificity of a genetic vaccine vector for a target cell.

14. (Twice Amended) A recombinant cell-specific binding moiety produced by expressing in a host cell a recombinant binding moiety-encoding nucleic acid obtained by the method of claim 2, wherein the recombinant cell-specific binding moiety comprises:

(i) a DNA binding domain derived from a protein selected from the group consisting of a transcriptional regulator, a polypeptide involved in DNA replication or recombination, a repressor, a histone, a protamine, an E. coli CAP protein, myc, a protein having a leucine zipper, a protein having a DNA binding basic domain, a protein having a POU domain, a protein having a zinc finger, and a protein having a Cys₃His (SEQ ID NO:6) box or the nucleic acid binding domain is an RNA binding domain derived from a protein selected from the group consisting of HIV tat and HIV rev; and

(ii) a cell-specific ligand that confers on the recombinant cell-specific binding moiety an enhanced ability to bind to the target cell, as compared to the cell-specific ligand encoded by the first and second forms of the additional nucleic acid.

16. (Twice Amended) A composition for eliciting an immune response that comprises a recombinant binding moiety-encoding nucleic acid obtained by the method of claim 2, wherein the recombinant cell-specific binding moiety comprises:

(i) a DNA binding domain derived from a protein selected from the group consisting of a transcriptional regulator, a polypeptide involved in DNA replication or recombination, a repressor, a histone, a protamine, an E. coli CAP protein, myc, a protein having a leucine zipper, a protein having a DNA binding basic domain, a protein having a POU domain, a protein having a zinc finger, and a protein having a Cys₃His (SEQ ID NO:6) box or the nucleic acid binding domain

is an RNA binding domain derived from a protein selected from the group consisting of HIV tat and HIV rev; and

(ii) a cell-specific ligand that confers on the recombinant cell-specific binding moiety an enhanced ability to bind to the target cell, as compared to the cell-specific ligand encoded by the first and second forms of the additional nucleic acid.

546 E² 17. (Twice Amended) A composition for eliciting an immune response that comprises:

- a) a recombinant binding moiety that comprises a nucleic acid binding domain and a cell-specific ligand, and
- b) a polynucleotide sequence that is capable of expressing an antigen and that comprises a binding site, wherein the nucleic acid binding domain is capable of specifically binding to the binding site.

3 18. (Three Times Amended) A method for producing and screening a recombinant cell-specific binding moiety for an ability to increase uptake, efficacy, or specificity of a vaccine or antigen for a target cell, the method comprising:

- (1) recombining at least first and second forms of at least one nucleic acid, wherein each of the first and second forms of the nucleic acid comprises a polynucleotide which encodes a binding moiety of an enterotoxin, wherein the first and second forms differ from each other in two or more nucleotides, to produce a library of recombinant nucleic acids;
- (2) producing a library of vectors from the library of recombinant nucleic acids, wherein each vector comprises a member of the library of recombinant nucleic acids;
- (3) introducing one or more members of the library of vectors into one or more host cells, wherein the member of the library of recombinant nucleic acids is expressed to form a recombinant cell-specific binding moiety polypeptide and recovering the recombinant cell-specific binding moiety polypeptide;
- (4) contacting the recombinant cell-specific binding moiety polypeptide with a cell surface receptor of a target cell; and
- (5) determining if the recombinant cell-specific binding moiety polypeptide exhibits enhanced ability to bind to the target cell.

506 E-3 51. (Amended) A method for producing and screening a recombinant cell-specific binding moiety polypeptide for an ability to increase uptake, efficacy, or specificity of a polypeptide antigen for a target cell, the method comprising:

(1) recombining at least first and second forms of at least one nucleic acid that comprises a polynucleotide which encodes a cell-specific binding moiety, wherein the first and second forms differ from each other in two or more nucleotides, to produce a library of recombinant nucleic acids;

D4 (2) introducing one or more members of a library of vectors, each of which comprises a member of the library of recombinant nucleic acids, into one or more host cells, wherein the member of the library of recombinant nucleic acids is expressed to form a recombinant cell-specific binding moiety polypeptide;

(3) contacting the recombinant cell-specific binding moiety polypeptide with a cell surface receptor of a target cell;

(4) determining if the recombinant cell-specific binding moiety polypeptide exhibits enhanced ability to bind to the target cell; and

(5) fusing or linking the recombinant cell-specific binding moiety polypeptide to the polypeptide antigen or coating the polypeptide antigen with the recombinant cell-specific binding moiety polypeptide.

D5 53. (Amended) The method of claim 51, wherein the recombinant cell-specific binding moiety polypeptide is fused or linked to the polypeptide antigen.

57. (Twice Amended) A method for producing a composition for eliciting an immune response, said method comprising coating the polypeptide antigen with a recombinant cell-specific binding moiety polypeptide produced by the method of claim 51.

D6 58. (Twice Amended) A composition for eliciting an immune response comprising an antigen and a recombinant cell-specific binding moiety polypeptide, wherein the composition is produced by the method of claim 51, wherein:

(i) the antigen comprises a polypeptide antigen;

(ii) the recombinant cell-specific binding moiety polypeptide exhibits enhanced ability to bind to the target cell; and

(iii) the polypeptide antigen and the recombinant cell-specific binding moiety polypeptide are derived from different polypeptides.

D⁶ 59. (Amended) The method of claim 2, wherein the binding site of each vector is derived from a binding site present in at least one form of at least one nucleic acid of (1).

D⁷ 61. (Amended) The method of claim 2, wherein the vector-binding moiety complex forms inside the host cell and, prior to the contacting of (5), the host cell is lysed under conditions that do not disrupt the vector-binding moiety complex.

62. (Amended) The method of claim 3, wherein the vector-binding moiety complex of (10) forms inside the host cell and, prior to the contacting of (11), the host cell is lysed under conditions that do not disrupt the vector-binding moiety complex.

65. A recombinant cell-specific binding moiety produced by expressing in a host cell a recombinant binding moiety-encoding nucleic acid obtained by the method of claim 2, wherein the recombinant cell-specific binding moiety comprises:

(i) a DNA binding domain; and

(ii) a cell-specific ligand that confers on the recombinant cell-specific binding moiety an enhanced ability to bind to the target cell, as compared to the cell-specific ligand encoded by the first and second forms of the additional nucleic acid.

D⁸ 66. A composition for eliciting an immune response that comprises a recombinant cell-specific binding moiety of claim 65.

67. A composition for eliciting an immune response that comprises a recombinant binding moiety-encoding nucleic acid obtained by the method of claim 2, wherein the recombinant cell-specific binding moiety comprises:

(i) a DNA binding domain; and

(ii) a cell-specific ligand that confers on the recombinant cell-specific binding moiety an enhanced ability to bind to the target cell, as compared to the cell-specific ligand encoded by the first and second forms of the additional nucleic acid

These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with the Examiner's position. In accordance with the requirements of 37 C.F.R. § 1.121, a marked up version of the claims showing the changes is attached as Appendix A. For the Examiner's convenience, a complete set of the currently pending claims is also provided as Appendix B.